

added new claims 95 and 95. Support for claim 95 and 96 can be found inter alia in the specification, e.g., at page 17, lines 25 to 32, and canceled claims 28 and 29.

Claims 1 to 23, 30 to 39, 45, 46, 59 to 66, 77 to 80, 85, 87 to 92, 95, and 96 are currently pending and under consideration in the application.

Provisional Obviousness-type Double Patenting Rejection:

In the March 2, 1999, Office Action, the Examiner provisionally rejected claims 1 to 23, 28 to 39, 45, 46, 59 to 66, 77 to 80, 85, and 87 to 92 under the "doctrine of obviousness-type double patenting as being unpatentable over claims 1 to 39, 45, and 46 of co-pending Application No. 08/822,774." Office Action at page 2, Item No. 3.

Since this is a provisional rejection and claims of neither case have been allowed, applicants request that this rejection be held in abeyance. At such time as allowable claims are indicated, applicants can then make a determination based on the allowed claims and the claims pending at the time whether a terminal disclaimer will be filed.

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1 to 23, 28 to 39, 45, 46, 59 to 66, 77 to 80, 85, and 87 to 92 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite "for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Office Action at Page 3, Item No. 4.

Specifically, the Examiner alleged that while the term "PEF" is defined in the specification as "purified naturally occurring polymerase enhancing factors and wholly

or partially synthetic copies or active analogs thereof [, ... the] scope of 'analog' is unclear." Id. The Examiner alleged that "[i]t is not clear how far one can diverge from the specific 'PEF' structure recited in the claims while still being considered a 'PEF' analog" Id. The Examiner suggested "[c]ancellation of the 'analog' portion of the definition." Id.

Applicants respectfully traverse the rejection. Applicants maintain that the cited claims are definite. As discussed in the specification, those skilled in the art are familiar with methods of generating analogs of proteins, e.g., mutating, modifying, truncating, or otherwise changing a protein's amino acid sequence and retaining its functional activity. Specification, e.g., at page 18, lines 3 to 12. Applicants assert that the knowledge of those skilled in the art combined with the teachings disclosed in the specification provide one skilled in the art would understand what is encompassed by the term "analog."

The Examiner rejected claim 28 because "[i]t is very difficult, if not impossible to determine ... the scope of a protein defined through 3 divergent functional definitions, one of them, the hybridization definition, is unrelated to protein function." Office Action at page 4, Item No. 4 B. The Examiner further contended that claims 1 to 20, 23, 29 to 39, 45, 59 to 66, 77 to 80, 85, and 87 to 92 are also indefinite because the scope of those claims is also defined using different unrelated schemes. Id. at page 4.

Without acquiescing to the Examiner's rejection and solely to expedite prosecution, Applicants have canceled claims 28 and 29. Accordingly, the §112, second paragraph, rejection concerning the scope of those claims is moot.

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To satisfy the requirements of the second paragraph of § 112, one of skill in the art must understand what is encompassed by a claim. Applicants maintain that one of skill in the art would understand what is encompassed by the pending claims as written.

With respect to claims 1 to 20, 23, 30 to 39, 45, 59 to 66, 77 to 80, 85, and 87 to 92, it is not clear from the rejection what terms are considered indefinite by the Examiner. Without having the specific alleged indefinite terms, Applicants are not able to respond. Accordingly, Applicants traverse this rejection with respect to those claims, and request that the Examiner provide specific alleged problems with the claims, if this rejection is maintained.

To the extent the Examiner rejects claims that define an amino acid sequence by the nucleotide sequence that encodes them or by a sequence that hybridizes to a complement of such a nucleotide sequence, applicants traverse such a basis for the rejection. In view of the genetic code, after one knows a particular nucleotide sequence, one will automatically know the amino acid sequence encoded by such a nucleotide sequence. Accordingly, it is appropriate to define amino acid sequences by the nucleotide sequences that encodes them.

The Examiner further rejected claims 1 to 23, 28 to 39, 45, 46, 59 to 66, 77 to 80, 85, and 87 to 92 because of the "recitation of 'or analogs thereof,' 'sequences hybridizable thereto,' 'degenerate variants thereof' and 'wholly or partially synthetic protein.'" Office Action at page 4, Item No. 4 C. The Examiner contended that "[e]ach of these limitations suggests that the claim is broader than the sequence or other

specific structure recited in the claims [, and there] is no way to determine how far from the recited protein one can drift and still be 'an analog' or a 'degenerate variant[.]'" Id.

Applicants respectfully traverse this rejection because those skilled in the art would understand the scope of the claimed invention. As discussed above, the specification provides those skilled in the art with the requisite knowledge to determine the scope of what is meant by "an analog." Specification, e.g., at page 18, lines 3 to 12. Further, those skilled in the art would comprehend the scope of what is meant by "wholly or partially synthetic protein." For example, the specification states that "[r]ecombinant PEF proteins, as a wholly synthetic copy of a naturally occurring protein, ... are also 'PEFs' according to this invention." Specification at page 17, lines 16 to 18. Further, those skilled in the art would know what is meant by "sequences hybridizable thereto." Techniques for the determination of sequences that hybridize to specific sequences were well known to those skilled in the art at the time of the filing of this application. However, to clearly define the claimed invention, Applicants have replaced "sequences hybridizable thereto" with "a sequence that hybridizes to the complement of the nucleotide sequence." Therefore, Applicants assert that claims reciting the phrases "an analog thereof" and 'wholly or partially synthetic protein' are clear.

Without acquiescing to the Examiner's rejection and solely to expedite prosecution, Applicants amended claims 12 and 17 by removing references to degenerate variants of the recited sequences. Accordingly, the §112, second paragraph, rejection concerning "degenerate variants" is moot.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §112, First Paragraph-Enablement

The Examiner rejected claims 1 to 20, 23, 28 to 39, 45, 59 to 66, 77 to 80, 85, and 87 to 92 under 35 U.S.C. §112, first paragraph, since the specification allegedly is not enabling. Office Action at pages 4 and 5, Item No. 5. Specifically, the Examiner alleged that "[t]he specification ... does not enable any person skilled in the art ... to make the invention commensurate in scope with these claims." Id. at page 5. The Examiner alleged that "[t]he claims are broadly drawn to protein activity [, analogs or variants, and] recite the source of the protein as 'bacterial, eukaryotic ... 'and thus broadly encompass both the animal and plant kingdoms. The specification, in contrast, merely discloses a single example, ... a UTPase protein from *Pyrococcus furiosus*." Id. The Examiner concluded that "[i]n view of the breadth of these claims, the small number of examples (one), the unpredictability of proteins and the lacking of guidance in the specification, it would require undue experimentation to enable a reasonable number of embodiments ...." Id.

Without acquiescing to the Examiner's rejection and solely to expedite prosecution, Applicants amended claim 1 to recite a polymerase enhancing protein obtained from an archael source. Accordingly, the §112, first paragraph, rejection concerning PEFs from plant and animal kingdoms is moot.

Applicants assert that the specification enables one skilled in the art to make and use a composition comprising a polymerase enhancing protein obtained from an archael source. The specification directs one skilled in the art to use techniques analogous to the specific examples involving polymerase enhancing proteins derived from *Pyrococcus furiosus* (Pfu) to obtain polymerase enhancing proteins from organisms other than Pfu. See specification, e.g., at page 17, line 25, to page 18, line 2. In view of that direction, one skilled in the art would look to Examples 1 to 4, and 7, which show techniques for obtaining polymerase enhancing proteins from Pfu that can be applied to other organisms and disclose tests for determining polymerase enhancing activity. See specification, e.g., page 20, line 1, to 27, line 23.

The Examiner has not established why one skilled in the art would require anything other than routine skills to obtain polymerase enhancing proteins from sources other than Pfu in view of the specification. Employing the reported procedures with organisms other than Pfu would require only routine skills and would not amount to undue experimentation.

Accordingly, the specification provides one of skill in the art with sufficient information to modify the disclosed procedures to obtain polymerase enhancing factors from other archael sources without undue experimentation. Therefore, Applicants assert that the Examiner has failed to establish that the specification does not enable those skilled in the art to practice the claimed invention of the rejected claims.

Further, Applicants assert that the specification enables those skilled in the art to make and use the claimed proteins. Based on the information in the specification

combined with what was known to those skilled in the art, making and using the claimed proteins would only require routine skills. Those skilled in the art are familiar with analogs of proteins, wholly or partial synthetic versions of proteins, and nucleic acids that encode proteins. The specification discloses further information that would enable those skilled in the art, e.g., at page 18, lines 5 to 12. Therefore, one of skill in the art would require only routine skills that do not amount to undue experimentation to make and use the claimed proteins.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the §112, first paragraph, rejection.

Rejection Under 35 U.S.C. §103

The Examiner rejected claims 1 to 20, 23, 28 to 39, 45, 59 to 66, 77 to 80, 85, and 87 to 92 under 35 U.S.C. §103 (a) for allegedly being obvious over Sorge et al., U.S. Patent No. 5,556,772 ("Sorge"). Office Action at page 6, Item No. 7. The Examiner alleged that "Sorge discloses ... compositions of matter, mixtures, kits, complexes and proteins isolated from . . . [*Pyrococcus*] furiosus, that enhances polymerase activity by increasing fidelity." Id. The Examiner contended that:

Sorge differs from claims 1-20, 23, 28-39, 45, 59-66, 77-80, 85 and 87-92 in the recitation of 'or analogs thereof,' 'degenerate variants thereof' and 'wholly or partially synthetic proteins,' proteins defined as encoded by DNA or 'sequences hybridizable thereto,' specific molecular weights and SEQ ID NO.'s and an antibody defined as binding the protein. Nevertheless, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions in the various manner claimed. Id.

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The Examiner alleged that "[t]hese differences are mere variations on a theme."

Id. The Examiner concluded that an ordinary artisan would have been motivated to repeat the purification method disclosed in Sorge and the "resulting extract [would] implicitly contain the naturally occurring protein complexes." Id. Further, the Examiner concluded that "Sorge discloses the cloning and sequencing of the *Pyrococcus furiosus* DNA polymerase. The ordinary artisan would have been motivated in claiming the nucleic acid sequence of the gene product ...." Id. at page 7. Finally, the Examiner contended that "the generation of an antibody from any protein is a matter of common knowledge. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to generate the antibody ...." Id.

Applicants respectfully traverse the rejection under 35 U.S.C. §103. Applicants disagree with the Examiner's contention that the claimed invention would have been an obvious variant of Sorge. Sorge discloses compositions which comprise polymerases. The present invention is directed to compositions containing proteins that are not polymerases. Rather, the proteins according to the present invention enhance polymerase activity. Sorge does not discuss factors that enhance polymerase activity.

Further, although the Examiner asserts that extract purified according to methods disclosed in Sorge would implicitly contain the naturally occurring protein complexes, the Examiner cites nothing in Sorge that either teaches or suggests such a conclusion. The Examiner cannot use the Applicants' disclosure of polymerase enhancing factors to supply information not discussed in Sorge. In *In re Sporman*, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966), the Court held that the "inherency of an advantage and its

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obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicted on what is unknown." (Emphasis added).

The holding in *Sporman* is directly applicable to the present situation. The Examiner has attempted to use an unknown but allegedly implicit characteristic, proteins that enhance polymerase activity, to show obviousness of a composition for enhancing polymerase activity. If one was unaware of the alleged presence of polymerase enhancing factors, what would have been the motivation to make a composition that enhances polymerase activity?

The Examiner also contends that Sorge would have rendered obvious the claimed nucleic acid sequences in claims 10 to 12, 17, and 20 to 23. Sorge discusses nucleic acids encoding polymerase. As discussed above, Sorge does not teach or suggest polymerase enhancing factor proteins. The presently claimed nucleic acid sequences encode polymerase enhancing factor proteins, not polymerases. The Examiner has failed to establish that a discussion of nucleic acids encoding polymerase would have rendered obvious nucleic acids that encode proteins that enhance polymerase activity. Thus, the Examiner has not established that the presently claimed nucleic acids would have been obvious in view of Sorge.

Further, the Examiner contended that Sorge would have rendered obvious the antibodies in claim 45. Since Sorge does not teach or suggest polymerase enhancing factor proteins, antibodies that bind such proteins would also not have been taught or suggested. The Examiner fails to establish how antibodies that bind polymerase

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enhancing factor proteins would have been obvious in view of a discussion of polymerase. Thus, the Examiner has not established that the claimed antibodies would have been *prima facie* obvious in view of Sorge.


Therefore, Applicants assert that Sorge would not have rendered obvious the claimed invention. Accordingly, Applicants request reconsideration and withdrawal of the obviousness rejection of the pending claims.

In view of the preceding remarks, Applicants respectfully request that the Examiner issue a timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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